Dermatoscopy in the evaluation of cutaneous lesions in patients with familial atypical multiple-mole melanoma syndrome

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ABSTRACT

Skin cancer is currently the most common cancer type afflicting North Americans today and with an aging population the incidence is likely to increase. Certain skin cancers such as melanoma can result in significant morbidity and mortality especially if not identified and treated early. The traditional ABCDE rule (*asymmetric shape, irregular borders, variation in colour, diameter >6 mm and evolution/elevation of the lesion*) used to identify concerning tumours will in fact miss many early melanomas. This problem is exacerbated in patients with hereditary forms of melanoma such as Familial Atypical Multiple-Mole Melanoma (FAMMM) syndrome where multiple atypical nevi satisfying the ABCDE criteria are present and would therefore warrant biopsy. Most of these biopsies would be unnecessary and would increase the patient's morbidity. Dermatoscopy is a clinical tool that provides a bridge between clinical and histopathologic evaluation and has proven to be helpful in triaging suspicious lesions in the general population and to be a first-line screening tool to increase the detection of early melanomas in patients with FAMMM.

INTRODUCTION

The incidence of melanoma has increased over the last few decades¹ and currently 1 in 57 to 1 in 74 Canadians are expected to develop the disease in their lifetime.² This is concerning as melanoma carries a poor prognosis unless identified and treated early.³ The causes of melanoma are multifactorial, with ultraviolet light as a major environmental risk factor.⁴ However, up to 12% of melanomas may be hereditary in nature.¹

FAMILIAL ATYPICAL MULTIPLE MOLE-MELANOMA (FAMMM) SYNDROME: DIAGNOSTIC CHALLENGE

Familial atypical multiple-mole melanoma (FAMMM) syndrome (also known as dysplastic nevus syndrome, atypical mole syndrome and B-K mole syndrome) is an example of a genetic syndrome with a strong association with the development of invasive melanoma. This clinical phenotype is defined by the National Institutes of Health Consensus (2002) as having greater than 50 melanocytic nevi, some dysplastic nevi with atypical histologic features and a family history of melanoma (Figure 1).^{1,5} In these patients, atypical or dysplastic nevi are more likely to undergo malignant transformation than benign-appearing nevi, however melanomas may develop de novo as well.¹

The most common genetic mutation in FAMMM is in the tumour suppressor gene CDKN2A, which may also increase the risk of other malignancies such as pancreatic cancer.⁵ Carriers of these mutations in North America have a 76% lifetime melanoma risk and are also more likely to develop more than one melanoma during their life.^{1,6} This makes routine skin surveillance very important in this patient population in order to identify melanomas early. However, FAMMM patients typically have multiple if not hundreds of phenotypically diverse nevi and many may be atypical in appearance.¹ These atypical nevi may be clinically concerning of melanomas and patients with FAMMM often require multiple skin biopsies to rule out invasive melanoma (Figure 1).⁷ More recently, dermatoscopy has been used as a tool to aid in the examination of skin lesions and may prevent unnecessary biopsies.

Figure 1. Patient with FAMMM with multiple atypical nevi.⁸

DERMATOSCOPY

Dermatoscopy is a clinical tool that is a real time in vivo link between clinical and histopathologic examination of the skin. It is a non-invasive procedure that magnifies lesions 10 times, which allows for quick evaluation of the morphological structures in the epidermis, dermoepidermal junction and papillary dermis.⁷ Originally coined the “dermatologist’s stethoscope,” the dermatoscope was first introduced to evaluate skin tumours, but it has also been proved useful to evaluate non-melanoma skin cancers, cutaneous infections and inflammatory skin.⁷

There are 2 major types of dermatoscopes available on the market: those using polarized light (PD) and those using non-polarized light (NPD). PD and NPD dermatoscopes have different uses and the information obtained from each type of dermatoscope is complementary.⁹ PD provides better visualization of deeper tissues, while NPD gives a better picture of more superficial structures.⁹

Newer technology has even made possible digital dermatoscopic monitoring (computer-assisted image analysis).^{9,10}

EFFICACY OF DERMATOSCOPY IN THE EVALUATION OF SKIN LESIONS

Currently the most common method of clinical assessment of a pigmented lesion is to visually inspect the lesion and apply the ABCDE assessment tool. The ABCDE rule, used to differentiate melanoma from benign nevi, utilizes a mnemonic device to identify concerning features (asymmetry in shape, irregularity of borders, variation in colour, diameter greater than 6 mm and elevation or changes in the lesion (evolution)). This tool has been shown to improve the early detection of melanoma.⁵ However, the morphological features identified by this mnemonic are more evident in larger melanomas and therefore smaller or early melanomas may appear benign until inspected dermatoscopically.⁵

The number needed to excise (NNE) is a useful metric for measuring the accuracy of melanoma detection and is calculated as the number of lesions excised per biopsy-proven melanoma diagnosis.⁵ Despite variations in clinical expertise, patient factors and lesional characteristics, dermatoscopy is associated with an improvement (decrease) in NNE. A recent meta-analysis found that dermatoscopy improves the clinician's diagnostic accuracy by 30% over that of unaided visual inspection alone.⁹ Therefore, dermatoscopy may decrease overall morbidity by avoiding excision and biopsy of benign lesions.⁵

DERMATOSCOPY IN PRACTICE: MANAGEMENT OF FAMMM

Patients with FAMMM may have numerous atypical nevi, the majority of which will not progress to melanoma.⁷ The optimal management strategy for patients with FAMMM involves total body photography, detailed dermatoscopic examination, and periodic monitoring.⁷ The dermatoscopic examination allows the clinician to identify and document the patient's unique pattern of atypical and benign nevi. Any changing lesions or those with concerning appearance under the dermatoscope should raise clinical suspicion even if they do not fulfill the ABCDE criteria. Instead, a 2-step clinical approach is suggested. The first step involves examination of the entire skin surface for any concerning pigmented lesions. In the second step, these abnormal lesions are evaluated more carefully. Dermatoscopic examination may reveal subtleties in shape, colour, contour and topography and can be used in conjunction with the ABCDE rule to determine whether the lesion should be biopsied.³

When using dermatoscopy a number of algorithms may be used to aid in detecting early forms of melanoma.¹¹⁻¹³ A common example is the ABCD rule that uses four dermatoscopic criteria: asymmetry (in one, two or no axes), border (sharp versus blurred demarcation in eight segments), colour (number of colours), and differential structures.⁹ The most common specific dermatoscopic structures suggestive of melanoma, include granularity, vascular changes and stromal changes.⁹ Granularity is estimated to be present in 94% of all melanomas as compared with 27% of benign lesions and refers to the presence of many blue-gray dots within a suspected neoplasm.⁹

Granularity, when present only in the periphery of the lesion with an irregular distribution or with red/white colouration, is particularly concerning for a diagnosis of melanoma.⁹ Granularity with a uniform appearance and/or involvement of less than 10% of the lesion suggests a benign lesion.⁹

PD does not require direct lesional contact for viewing epidermal and subepidermal structures, and therefore pressure that causes blanching of vasculature can be avoided.³ PD is therefore well suited for viewing dermal vessels, which can take on specific morphologies associated with melanoma. Dotted vessels for example, which appear as tiny red dots, confer a positive predictive value of 90% for melanocytic tumours.³ Features such as linear vasculature with irregularity in size and shape, as well as milky red globules, are also characteristically associated with melanoma.⁹ If the majority of the tumour under dermatoscopy has pinkish hue or erythematous blush this is also a predictor of invasive melanoma.⁹

DERMATOSCOPY IN FAMILY PRACTICE

Dermatoscopy is not only used worldwide by dermatologists, but is also gaining rapid acceptance by general practitioners and surgeons.⁷ Family doctors are front line care providers and have a vital role in education, prevention and screening for skin cancers. In fact it has been documented that most skin cancers are detected by family doctors rather than specialists.³ Research studying the use of dermatoscopy by family practitioners is scarce, however a recent randomized trial reported family physicians who received a two day training course on dermatoscopy achieved better referral sensitivity when evaluated after 3 months (55% to 80%).³ This suggests that family practitioners can effectively use dermatoscopy to evaluate skin lesions and potentially decrease the number of unnecessary expert referrals.³

LIMITATIONS OF DERMATOSCOPY AND CONCLUSIONS

Overall, dermatoscopy has proven to be a valuable tool for evaluating a variety of dermatoses. Dermatoscopy has been shown to be a particularly useful tool for managing patients with FAMMM, where the presence of numerous atypical nevi presents diagnostic challenges. However, dermatoscopy is not without its disadvantages; it can be a costly instrument and does require training to allow for accurate interpretation of findings.⁹ About 80% of melanomas are estimated to be recognized on the basis of their clinical or dermatoscopic characteristics, leaving up to 20% that may be erroneously deemed benign on first assessment.⁹ While the beneficial role of dermatoscopy in improving melanoma diagnosis is clear, it should not be relied on solely, as some lesions may still be misdiagnosed, due to unique morphological characteristics or presentation. Certain melanoma subtypes are more prone to misdiagnosis including lentigo maligna, nodular melanoma and amelanotic melanoma.^{9,14} Uptake of dermatoscopy may also be limited by time required to use the tool, as it is estimated to take double the time compared to an unaided visual examination.⁵ Nonetheless, a thorough complete skin examination with dermatoscopy can be completed in a reasonable amount of time (approximately 5 minutes)

and may potentially help differentiate benign lesions from clinically concerning skin cancer.⁵

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